VII. Executive Summary

BACKGROUND This report presents results of a 24 month study of human response to two-hour exposures to freeway air in Southern California. Numerous epidemiological studies have linked increases in particulate matter exposure to increases in cardiovascular mortality and morbidity. Some evidence has been published recently that supports the hypothesis that particulate matter and gases associated with diesel exhaust are associated with acute clinical and biological effects. Moreover, although supporting data are more limited than data on PM-2.5, concentrated ambient ultrafine particles (diameter <100 nm) are associated with pulmonary and cardiovascular effects, and ambient ultrafine PM is weakly associated with adverse cardiovascular events. A recent study found that the relative risk of myocardial infarction was increased two to threefold by time spent in traffic one or two hours prior to the onset compared with control periods. There are no systematic measurements of ultrafine particles inside vehicles and their associated human health effects during commuting. However, exposure to ultrafine particles is known to be substantially elevated during travel on freeways. The primary objectives of the present study were to document acute effects in late middle-aged and elderly volunteers riding on Los Angeles freeways, and to relate these effects to specific air pollution components. This study contributes to exposure assessment of freeway commuters and the establishment of standards for ultrafine particles associated with freeways.

METHODS The study used a modified nine-passenger van with an exposure chamber and filtration system to expose a total of 19 clinically healthy subjects, aged 61 to 83, for two hours each to either unfiltered or filtered freeway air on two freeways, one with mostly gasoline vehicles (I-405) and the other with a high proportion of heavy-duty diesel trucks (I-710). The filtration system delivered the unfiltered or filtered (96% of particles removed) air to the exposure chamber inside the van. The exposure chamber could accommodate two subjects. State-of-the-art instruments were used to measure concentration and size distribution of fine and ultrafine particles and the concentration of carbon monoxide (CO), carbon dioxide (CO_2), black carbon (BC), particle bound polycyclic aromatic hydrocarbons (PB-PAHs), PM-10 mass, PM-2.5 mass, and oxides of nitrogen (NOx) in near-real time in the subject's breathing zone inside the exposure chamber.

Measures of cardiovascular health included: 24-hour ambulatory ECG for the assessment of heart rate variability and incidence of ectopic heart beats; blood pressure, heart rate – blood pressure product, lung function, and blood biochemistry to assess systemic inflammatory markers (fibrinogen, IL-6, CRP, MPO, MCP-1); vascular response or injury (sE-selectin, VEGF, sVCAM, sICAM, MMP9, MPO, t-PAI-1), and myocardial response to hemodynamic changes (NT-proBNP). Cardio-respiratory symptoms were monitored before and after exposures to detect immediate and acute health effects. Subjects, and those doing the health monitoring and biochemical and electrical signal analysis, were blinded as to the type of exposure.

RESULTS Average total particle number concentration, as measured by a condensation particle counter (CPC), of unfiltered air inside the enclosure was 77,800 and 107,500 particles/cm^3 on the I-405 and the I-710 freeway, respectively. The highest one-minute averaged particle number concentration was 730,000 particles/cm^3 on the I-710 freeway. Bimodal size distributions were typical for both freeways, with the first mode around 12–20 nm and the second mode around 50–100 nm. BC and particle-bound PAH concentrations were more than two times greater on the I-710 than on the I-405 freeway. Ultrafine particles represented about 36 to 76% of total particle number concentrations on I-405, and 56% to 84% on I-710. A peak in average particle number concentration of 125,000 particles/cm^3 was associated with a traffic speed of 40 to 50 mph. Whereas most health endpoints did not vary significantly by freeway or filter condition, atrial ectopic beat incidence during and after exposure decreased 20% on average with filtered versus unfiltered air ($P<0.05$). Between-freeway differences were non-significant, but individual responses related more strongly to particle count ($P=0.01$), PAH ($P=0.02$) and black carbon ($P=0.04$) than to mass ($P=0.07$). N-terminal pro B-type natriuretic peptide (NT pro-BNP) and vascular endothelial growth factor (VEGF) decreased 30% on average in filtered compared to unfiltered air ($P<0.05$).

DISCUSSION These findings indicate that breathing unfiltered freeway air, as compared to breathing filtered air, triggers an increase in supraventricular ectopic beats, and that this increase is associated with a statistically significant increase in NT pro-BNP relative to NT pro-BNP levels measured in the absence of filtration. The association of an increase in supraventricular ectopic beats with an increase in NT pro-BNP

implicates an increase in intra-atrial pressure, or stretch, as the underlying mechanism for the increase in arrhythmia. Such an effect is speculated to be related to direct or indirect effects on traffic related particles on pulmonary artery pressure or atrial mechanical function. The relative increase in VEGF after breathing unfiltered air suggests an injury response of the vascular endothelium. Such a response is most likely to occur in the lung as this is the point of entry of the particles. A local pulmonary vascular response, e.g. secondary to the release of endothelin-1 might evoke a vasoconstriction with an attendant increase in intrapulmonary pressures and subsequently increased pressures in the right heart and release of NT pro-BNP.

While the absolute number of supraventricular ectopic beats initiated in this study is low and not clinically relevant in healthy individuals, it does suggest that such a trigger when applied to hearts with more advanced disease might yield more complex and sustained arrhythmia like those observed in individuals having coronary heart disease or heart failure. As such, the observation in this study that traffic related particulate pollution increases supraventricular ectopic beats might have important public health implications, in that supraventricular ectopic beats initiate a wide variety of atrial and atrioventricular arrhythmias. For example, atrial fibrillation is the most common serious arrhythmia in late middle age and elderly populations. It contributes to poor quality of life, stroke, myocardial infarction and heart failure. Likewise less serious, yet still debilitating arrhythmia, such as atrial tachycardia, AV nodal reciprocating tachycardia, and AV nodal tachycardias are initiated by premature beats.

Health responses were not clearly different between the diesel-truck-dominated freeway and the gasoline-car dominated freeway, and exposure concentration ranges on the two freeways overlapped considerably. However, the significant association of unfavorable responses with PM number concentration, particularly in the ultrafine size range, PAH and black carbon along with the tendency for more PM emissions from diesel engines, argues that diesel-truck traffic presents the greater cardiovascular health hazard.

CONCLUSIONS This study documents a cardiac and vascular response associated with freeway travel that provides new insight into the association of inhalation of traffic related pollutants to arrhythmia. In our relatively healthy (age > 60) adult volunteers, exposure to particulate matter on freeways was associated with a small but statistically significant increased incidence of atrial arrhythmia, but with generally stable or decreased incidence of ventricular arrhythmia and generally stable heart rate variability. Concurrent relative increases in NT pro-BNP and VEGF suggest that increased intra-atrial pressure triggered atrial arrhythmia and might be mechanistically linked to pulmonary vascular injury and attendant vasoconstriction. Effects appeared to relate to black carbon, PAH, and the ultrafine particulate fraction. Particle count was strongly correlated with arrhythmia incidence while PM-2.5 and PM-10 mass concentrations were not significantly correlated with arrhythmia incidence. Rigorous double-blind conditions and filtered-air controls in this study, rule out other traffic-related stresses or pollutant gases as causes of the particulate matter-associated cardiovascular effects. Because sustained arrhythmias (e.g. atrial fibrillation, AV nodal reentrant tachycardia) are triggered by premature atrial beats, traffic exposure may play a role in their occurrence - a risk that could be mitigated by filtering particulate matter from the vehicle passenger cabins. These results will aid the Air Resources Board in evaluating the importance of motor-vehicle related ultrafine particles. They will also contribute to the evidence needed for the development of a number-based standard for ultrafine particles. These conclusions could be strengthened by additional studies using more subjects, subjects with pre-existing cardiovascular conditions, and by focusing on ultrafine particles and black carbon and particulate PAH compounds.